

I. NEW ACRIDINE DERIVATIVES ANALOGOUS TO
ATEBRINE

II. MONOCROTALINE ANALOGS

BY

MING-CHIEN CHIANG

B.S., National University of Peking, 1935

M.S., University of Maryland, 1943

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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CHEMISTRY IN THE GRADUATE SCHOOL OF
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I. NEW ACRIDINE DERIVATIVES ANALOGOUS TO ATEBRINE

II. MONOCROTALINE ANALOGS

The intensive search in many laboratories to find a synthetic antimalarial with more favorable properties than plasmochin or atebrine has led the author to a study of some new acridine derivatives analogous to atebrine and of some monocrotaline analogs. In the former series, compounds with a phenyl group in the 4-position of the atebrine molecule or its analogs have been synthesized and, in the latter series, mono- and di-esters of retronesine and platynecine with aliphatic and aromatic acids have been prepared.

The synthesis of 4-phenylatebrine has been accomplished by the following series of reactions:

- (1) Condensation of 2-aminobiphenyl with 2,4-dichlorobenzoic acid in the presence of a copper catalyst in an alkaline medium to form 2'-phenyl-2-carboxy-5-chloro-diphenylamine,
- (2) Cyclization of the amine by action of phosphorus oxychloride to form 4-phenyl-6-chloroacridone,
- (3) Nitration of the acridone with dilute nitric acid in glacial acetic acid to 2-nitro-4-phenyl-6-chloroacridone,
- (4) Reduction of the nitroacridone to the corresponding aminoacridone by stannous chloride and concentrated hydrochloric acid in an alcoholic solution,
- (5) Diazotization of the aminoacridone to the diazonium chloride which, upon treatment with fluoboric acid, forms the 2-diazonium fluoborate of 4-phenyl-6-chloroacridone, and upon treatment with sodium acetate forms the 2-diazoimino derivative,
- (6) Conversion of the 2-diazonium fluoborate or the 2-diazoimino derivative of 4-phenyl-6-chloroacridone into 2-hydroxy-4-phenyl-6-chloroacridone by boiling with dilute sulfuric acid,
- (7) Methylation of the hydroxy compound with dimethyl sulfate to form 2-methoxy-4-phenyl-6-chloroacridone,

(8) Chlorination of the acridone to 2-methoxy-4-phenyl-6,9-dichloroacridine by treatment with phosphorus pentachloride,

(9) Conversion of the 9-chloro compound to the corresponding 9-phenoxy derivative by heating with phenol, and

(10) Condensation of the phenoxy acridine with δ -diethylamino- α -methylbutylamine to form 2-methoxy-4-phenyl-6-chloro-9-(δ -diethylamino- α -methylbutylamino)-acridine or 4-phenylate-brine.

4-Phenyl-6-chloro-9-(δ -diethylamino- α -methylbutylamino)-acridine has been prepared in a similar manner.

In the second series, some mono- and di- acetyl, propionyl and benzoyl derivatives of retronecine and platynecine have been synthesized. The direct esterification of the retronecine and platynecine bases with an acyl halide in an anhydrous medium and subsequent purification of the ester hydrohalides from anhydrous solvents has been found to give the most satisfactory results. The acetyl and benzoyl derivatives of retronecine and platynecine which were synthesized showed no antimalarial activity.

VITA

The author was born on November 11, 1911, in Pengsi, Szechwan, China. He attended the District Primary School and the District Junior Middle School of Pengsi. In 1929 he entered the Preparatory School of the National University of Peking, Peiping, China. In 1931 he was allowed to enter the Chemistry Department of that University, from which Department he was graduated in June, 1935, with the degree of Bachelor of Science. During his junior year he held a University Scholarship and the senior year a Yang Lien-Fu Memorial Scholarship. From 1935 to 1940 he was assistant in chemistry and from 1940 to 1941 instructor in chemistry in the National University of Peking. After a competitive examination he was granted a National Tsing-Hua University Fellowship to pursue advanced studies in the United States. He arrived in the United States in October, 1941, and was enrolled in the Graduate School of the University of Maryland, from which he received the degree of Master of Science in February, 1943. Since September, 1942, he has been enrolled in the Graduate School of the University of Illinois. He held a university scholarship from February, 1943, to June, 1944. He is a member of the Chinese Chemical Society, Phi Lambda Upsilon and Sigma Xi honorary fraternities. The following are his more important chemical publications:

Tseng, Hu and Chiang, Determination of Organic Halogens. I. Parr Bomb Method, *J. Chinese Chem. Soc.*, **3**, 39-51 (1935).

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Hsueh and Chiang, Periodic Properties of Elements, *J. Chinese Chem. Soc.*, **5**, 263-85 (1937).

